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10/518,927	12/23/2004	Helmut Fiebig	MERCK-2966	8085

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ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,927	FIEBIG ET AL.	
	Examiner	Art Unit	
	Nora M. Rooney	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,15,16 and 20-25* is/are pending in the application.

4a) Of the above claim(s) *1-12 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13, 15 and 20-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/23/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Sequence alignment*.

DETAILED ACTION

1. Claims 1-13, 15-16 and 20-25 are pending.

2. Applicant's election with traverse of Group II, claims 13-15 in the reply filed on 06/29/2007 and the species of SEQ ID NO:1 in the reply filed on 08/24/2007 is acknowledged. The traversal is on the ground(s) that no explanation was provided, and moreover, the Office Action does not provide scientific evidence as to how Fischer et al. teach and/or suggest the Phl p 4 protein of the instant invention. Applicants argue that the claims in the instant application involve related subject matter, for example, a grass pollen allergen, as recited in Applicants' elected Group II. All the claims would comprise overlapping subject matter and it would not be an undue burden on the Examiner to carry out a search.

This is not found persuasive because the Examiner explained that Fischer et al. teaches the characterization of the Phl p4 polypeptide from Phleum pratense. The claims of Group II are drawn to the Phl p 4 polypeptide. Therefore, those claims are anticipated, thereby making the claims lack unity of invention.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 1-12 and 16 and are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Groups, there being no allowable generic or linking

claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 06/29/2007.

4. Claims 13, 15 and 20-25 are currently under examination as they read on a polypeptide encoded by the nucleic acid sequence of SEQ ID NO:1 and a pharmaceutical composition or vaccine thereof.

5. Applicant's IDS document submitted on 12/23/2004 is acknowledged. However, none of the references have been received in the application, so they were not considered.

Claim Objections

6. Claims 20 and 25 are objected to because of the following informalities:

Claim 25 is dependent upon cancelled claim 14.

Claim 20, the word "vaccine" is misspelled in that it has a space between v and a.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 13, 15 and 20-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 recites "fragment 1-200", "amino acids 1-200 of Phl p 4", "fragment 185-500"; and "amino acids 185-500 of Phl p 4" without reference to a specified sequence identification number making the claim indefinite. The recitation of positions within the Phl p 4 protein is indefinite without a reference sequence to which it refers.

The recitation of "a polypeptide encoded by a polynucleotide sequence which hybridizes to the complement of the polynucleotide sequences in (c) under stringent conditions" in claim 13 is ambiguous. Although the specification discloses general parameters for calculating such conditions, in the absence of a clear definition of the metes and bounds of this phrase it is unclear which conditions are actually claimed. It is suggested that Applicant amend the claims to recite a particular set of hybridization and wash conditions to overcome this rejection.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 13, 15 and 20-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: polypeptides of SEQ ID NO: 2, 4, 6 encoded by SEQ ID NO:1, 3 or 5, respectively and a composition thereof, does not reasonably provide enablement for: A polypeptide which **comprises** (a) a polypeptide whose sequence is set forth in SEQ ID NO: 2, SEQ ID NO: 4 or SEQ ID NO: 6, (b) a polypeptide **comprising a mutation, elimination or addition of at least one amino acid residue** in the polypeptide sequence set forth in (a), (c) a polypeptide which is encoded by a polynucleotide whose sequence is set forth in SEQ ID NO: 1, SEQ ID NO: 3 or SEQ ID NO: 5, or (d) a polypeptide which is **encoded by a polynucleotide sequence which hybridizes to the complement of the polynucleotide sequences in (c) under stringent conditions and originates from DNA sequences of Poaceae species** (e) a polypeptide which is **encoded by a single nucleotide polymorph of the polynucleotide sequence set forth in (c)**, wherein each of the polypeptides of (a) to (e) is immunogenic and induces an immunomodulatory T-cell reactive response in a host of claim 13; a pharmaceutical composition comprising **at least one polypeptide according to Claim 13** and a pharmaceutically acceptable carrier of claim 15; A vaccine comprising **a polypeptide of claim 13** and an acceptable carrier, wherein said vaccine is capable of generating an immunomodulatory, T-cell response in a host of claim 20; An **immunomodulatory, T-cell-reactive fragment of a group 4 *Poaceae* allergen** which **comprises** a **partial sequence or a combination of partial sequences of at least one polypeptide of claim 13** of claim 21; The immunomodulatory, T-cell-reactive fragment of a group 4 *Poaceae* allergen according to claim 21 which is (a) **fragment 1-200, with amino acids 1-200 of Phi p 4, or (b) fragment 185-500, with amino acids 185-500 of Phi p 4** of claim 22; the polypeptide according to Claim 13 (b),

wherein said **mutation results in the replacement of at least one cysteine residue** of a polypeptide whose sequence is set forth in SEQ ID NO: 2, SEQ ID NO: 4 or SEQ ID NO: 6 with **another amino acid residue** of claim 23; The polypeptide according to Claim 13 (d), which comprises **replacement of at least one cysteine residue of the polypeptide** which is encoded by a polynucleotide whose sequence is set forth in SEQ ID NO: 1, SEQ ID NO: 3 or SEQ ID NO: 5 with **another amino acid residue** of claim 24; An immunotherapeutic vaccine comprising **a polypeptide of claim 14** and an acceptable carrier, wherein said vaccine is capable of generating an immunomodulatory, T-cell response in a host.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not provide a sufficient enabling description of the claimed invention. The specification discloses only the nucleic acid sequences SEQ ID NO:1, 3 and 5 encoding the polypeptides of SEQ ID NO:2, 4 and 6, respectively.

The instant claims encompass in their breadth:

1.) the polypeptide of SEQ ID NO:2, 4, or 6 encoded by SEQ ID NO:1, 3 or 5, respectively.

2.) *any* fragment or combination of fragments of the polypeptides of SEQ ID NO:2, 4 or 6 encoded by SEQ ID NO:1, 3 or 5;

3.) any polypeptide "comprising" a fragment or combination of fragments of the polypeptides of SEQ ID NO:2, 4 or 6 or encoded by SEQ ID NO:1, 3 or 5 or the complement thererof.

4.) any polypeptide encoded by: the polynucleotide or any subsequence of SEQ ID NO:1, 3 or 5, a polynucleotide or any subsequence that binds the complement of SEQ ID NO:1, 3 or 5, or any polynucleotide that encodes a nucleotide polymorph of the SEQ ID NO:1, 3, or 5; and

5.) any polypeptide mutant of the polypeptides of SEQ ID NO:2, 4 or 6 or encoded by SEQ ID NO:1, 3, 5 or a polynucleotide that binds the complement of SEQ ID NO:1, 3 or 5 having any number of undisclosed mutations, deletions and additions.

There is insufficient guidance in the specification as filed as to how the skilled artisan would make the various nucleic acids and proteins recited in the instant claims. A person of skill in the art would not know which sequences are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences. There is insufficient guidance to direct a person of skill in the art to select particular sequences or sequence lengths as essential for the claimed functions. Without detailed direction as to which nucleic acid sequences are essential to the function of the encoded polypeptide, a person of skill in the art would not be able to determine without undue experimentation which of the plethora of polynucleotide, protein and

peptide sequences encompassed by the instant claims would exhibit the claimed functional characteristics, of being immunogenic and induces an immunomodulatory T-cell reactive response in the host other than the polypeptides of SEQ ID NO:2, 4 and 6 encoded by the nucleic acids of SEQ ID NO:1, 3 and 5.

The art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases and recognized that it was unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences. Even single amino acid differences can result in drastically altered functions between two proteins. For example, Metzler et al. teaches that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (PTO-892, Reference U; in particular, Table 2). Bowie et al. teaches that determination of three-dimensional structure from primary amino acid sequence, and the subsequent inference of detailed aspects of function from structure is extremely complex and unlikely to be solved in the near future (PTO-892, Reference V; page 1306 in particular). Thus, it is highly unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

In view of this unpredictability; the skilled artisan would not reasonably expect a polypeptide having anything less than 100% identity *over the full length of SEQ ID NO:2, 4 or 6* to *share the same function* as the polypeptide of SEQ ID NO:2, 4 or 6. The limitation "wherein each of the polypeptides of (a) to (e) is immunogenic and induces an immunomodulatory T-cells

reactive response in a host" is not seen as providing a requisite functional activity since numerous functional activities are encompassed by the specification and claims. The specification does not provide sufficient guidance as to which amino acids may be substituted, deleted, inserted and/or added and still retain the requisite function.

There is insufficient guidance in the specification regarding which partial sequences or combination of partial sequences of SEQ ID NO:2, 4 or 6 are immunomodulatory and T cell-reactive. The term immunomodulatory implies that the immune system is changed, but no specific changes are recited. Therefore, the term immunomodulatory encompasses just about any reaction by any cells or pathways related to the immune system. In the same way, the term 'T-cell reactive' is largely undefined. Any fragment or processed subsequence of the fragment that induces any T cell response or interaction is encompassed by the instant claims.

The specification does not provide support for any polypeptide "comprising" (b) a polypeptide comprising a mutation, elimination or addition of at least one amino acid residue in the polypeptide sequence set forth in (a) or (d) a polypeptide which is encoded by a polynucleotide sequence which hybridizes to the complement of the polynucleotide sequences in (c) under stringent conditions and originates from DNA sequences of Poaceae species (e) a polypeptide which is encoded by a single nucleotide polymorph of the polynucleotide sequence set forth in (c), wherein each of the polypeptides of (a) to (e) is immunogenic and induces an immunomodulatory T-cell reactive response in a host of claim 13. The term 'comprising ' is open language. As written, the claim encompasses an enormous number of undisclosed

polypeptides and peptides that may include sequence that is unrelated to the polypeptides of SEQ ID NO:2, 4 or 6 or encoded by SEQ ID NO:1, 3, 5 that could independently posses the requisite function.

Further, the fact that two nucleic acid sequences will hybridize under stringent conditions does not in and of itself require that the two sequences share any functional activity. Thus the same observations apply to the recitation of "a polynucleotide which hybridizes to the complement of the polynucleotide sequences in (c) under stringent conditions and originates from DNA sequences of Poaceae species." It was well known in the art at the time the invention was made that hybridization could occur between two sequence based upon short stretches of 100% identity. Thus a great deal of sequence variability *with respect to the full-length nucleic acid* is possible. Thus as for the recitation of hybridization language in the absence of *a testable function* and limitations regarding both the *hybridization conditions* and the *sequence length over which the hybridization takes place*; does not allow the skilled artisan to make and use the hybridizing nucleic acids commensurate in scope with the instant claims without undue experimentation.

The instant claims encompass subsequences of SEQ ID NO:1, 3 and 5 because the claim language does not require that the nucleic acids encode the full length sequences set forth in SEQ ID NO:2, 4 or 6. Rather, the claims encompass any amino acid sequence comprising either the full length of SEQ ID NO:2, 4 or 6 or any subsequence thereof or any nucleic acid encoding any subsection of SEQ ID NO:2, 4 or 6 . The specification does not provide sufficient guidance as to

which subsequences of SEQ ID NO:2, 4 or 6 would be immunogenic and induce an immunomodulatory T-cell reactive response in a host. The specification does not appear to have provided any working examples of any functional subsequences. Thus, it would require undue experimentation of the skilled artisan to determine which subsequences of SEQ ID NO:2, 4 or 6 and nucleic acids encoding SEQ ID NO:2, 4 or 6, including fragments, would have the function of the full length molecule, and in turn identify nucleic acid subsequences of SEQ ID NO:1, 3 o5 which encode these subsequences. There is insufficient support in the specification for any subsequence of SEQ ID NO:2, 4 or 6.

Also at issue is whether or not the claimed composition would function as pharmaceutical composition and/or vaccine. In view of the absence of a specific and detailed description in Applicant's specification of how to effectively use the pharmaceutical composition or vaccine as claimed, absence of working examples providing evidence which is reasonably predictive that the claimed pharmaceutical compositions or vaccine are effective for in vivo use, and the lack of predictability in the art at the time the invention was made, an undue amount of experimentation would be required to practice the claimed pharmaceutical composition with a reasonable expectation of success.

Further, a vaccine is a composition to induce specific immunity that **prevents** or protects against a specific disease caused by a specific agent. The first criterion in judging a vaccine is the level of antibody (humoral immune response) before and after immunization. The success of the vaccination is judged by the extent of increase in the level of antigen - specific antibody. The

second criterion for a vaccine is its ability to stimulate memory T lymphocytes (cell-mediated immune response) (See Immunology, Kuby, Fourth Edition, Chapter 18 in particular, PTO-892 Reference W). The specification provides no information on the vaccine formulation comprising any polypeptide, derivative or fragment of SEQ ID NO:2, 4 or 6 which is able to exhibit antigen-specific antibody response, stimulated memory T lymphocytes and to protect or prevent against allergy. Vaccines by definition trigger an immunoprotective response in the host vaccinated and a mere antigenic response is insufficient. Further at issue is whether or not the claimed method would function to "prevent" allergy. The specification provides no in vivo data to support the claimed subject matter. The specification fails to provide guidance as to how to totally prevent (100% prevention) allergy using a vaccine or pharmaceutical composition comprising any polypeptide, derivative or fragment of SEQ ID NO:2, 4 or 6. The invention may reduce the likelihood of an allergy by administering the compound of SEQ ID NO:2, 4 or 6, but the specification does not disclose how to totally prevent allergy. Therefore, the specification does not provide sufficient guidance on how to sufficiently prevent the occurrence of allergy by administering the claimed compound.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, the changes which can be made in the instantly recited nucleic acid sequences and still encode a polypeptide that maintains the functional properties of the polypeptide of SEQ ID NO:1 is unpredictable, as is the identity of which subsequences would encode a functional polypeptide; thus the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

11. Claims 13, 15 and 20-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of the polypeptides of SEQ ID NO: 2, 4, 6 encoded by SEQ ID NO:1, 3 or 5, respectively and a composition thereof.

Applicant is not in possession of a polypeptide which **comprises** (a) a polypeptide whose sequence is set forth in SEQ ID NO: 2, SEQ ID NO: 4 or SEQ ID NO: 6, (b) a polypeptide **comprising a mutation, elimination or addition of at least one amino acid residue** in the polypeptide sequence set forth in (a), (c) a polypeptide which is encoded by a polynucleotide whose sequence is set forth in SEQ ID NO: 1, SEQ ID NO: 3 or SEQ ID NO: 5, or (d) a polypeptide which is **encoded by a polynucleotide sequence which hybridizes to the complement of the polynucleotide sequences in (c) under stringent conditions and originates from DNA sequences of Poaceae species** (e) a polypeptide which is **encoded by a single nucleotide polymorph of the polynucleotide sequence set forth in (c)**, wherein each of the polypeptides of (a) to (e) is immunogenic and induces an immunomodulatory T-cell reactive response in a host of claim 13; a pharmaceutical composition comprising **at least one polypeptide according to Claim 13** and a pharmaceutically acceptable carrier of claim 15; A vaccine comprising **a polypeptide of claim 13** and an acceptable carrier, wherein said vaccine is

capable of generating an immunomodulatory, T-cell response in a host of claim 20; An **immunomodulatory, T-cell-reactive fragment of a group 4 *Poaceae* allergen** which **comprises a partial sequence or a combination of partial sequences of at least one polypeptide of claim 13** of claim 21; The immunomodulatory, T-cell-reactive fragment of a group 4 *Poaceae* allergen according to claim 21 which is (a) **fragment 1-200, with amino acids 1-200 of Phi p 4, or (b) fragment 185-500, with amino acids 185-500 of Phi p 4** of claim 22; the polypeptide according to Claim 13 (b), wherein said **mutation results in the replacement of at least one cysteine residue** of a polypeptide whose sequence is set forth in SEQ ID NO: 2, SEQ ID NO: 4 or SEQ ID NO: 6 with **another amino acid residue** of claim 23; The polypeptide according to Claim 13 (d), which comprises **replacement of at least one cysteine residue of the polypeptide** which is encoded by a polynucleotide whose sequence is set forth in SEQ ID NO: 1, SEQ ID NO: 3 or SEQ ID NO: 5 with **another amino acid residue** of claim 24; An immunotherapeutic vaccine comprising **a polypeptide of claim 14** and an acceptable carrier, wherein said vaccine is capable of generating an immunomodulatory, T-cell response in a host.

Applicant has disclosed only the polypeptides of SEQ ID NO: 2, 4, 6 encoded by SEQ ID NO:1, 3 or 5, respectively and a composition thereof; therefore, the skilled artisan cannot envision all the contemplated nucleic acid sequence possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that

it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claims 13, 15, 20-21 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Fischer et al. (PTO-892 mailed on 06/07/2007, Reference U).

Fischer et al teaches isolation of the allergen Phl p 4 from Phleum pratense and a decapeptide thereof (T cell reactive fragment) in a pharmaceutically acceptable carrier (Tris-buffered saline or water) (In particular, 'Methods' section on pages 190-192, whole document).

The recitations of "a polypeptide which comprises (a) a polypeptide whose sequence is set forth in SEQ ID NO: 2, SEQ ID NO: 4 or SEQ ID NO: 6, (b) a polypeptide comprising a mutation, elimination or addition of at least one amino acid residue in the polypeptide sequence set forth in (a), (c) a polypeptide which is encoded by a polynucleotide whose sequence is set

forth in SEQ ID NO: 1, SEQ ID NO: 3 or SEQ ID NO: 5, or (d) a polypeptide which is encoded by a polynucleotide sequence which hybridizes to the complement of the polynucleotide sequences in (c) under stringent conditions and originates from DNA sequences of Poaceae species (e) a polypeptide which is encoded by a single nucleotide polymorph of the polynucleotide sequence set forth in (c), wherein each of the polypeptides of (a) to (e))" of claim 13 and :which comprises a partial sequence or combination of partial sequences of at least one polypeptide" of claim 21 are inherent features of the reference polypeptide. Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999) "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art... However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. " The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art". Further, the complement of the DNA encoding the reference Phl p 4 polypeptide would hybridize under stringent conditions with the polypeptide of SEQ ID NO:2, 4 or 6.

The functional limitations "that is immunogenic and induces an immunomodulatory T-cell reactive response in a host" of claim 13; "wherein said vaccine is capable of generating an immunomodulatory, T-cell response in a host" of claim 20; "An immunomodulatory, T-cell-reactive fragment of a group 4 *Poaceae* allergen" of claim 21; and "wherein said vaccine is capable of genrating an immunomodulatory, T-cell response in a host" are inherent properties of the reference allergen, allergen fragment and compositions thereof. Where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may be an inherent characteristic of the prior art, it has the authority to require the

applicant to prove that the subject matter shown in the prior art does not possess the characteristics relied on. In re Schreiber, 44 USPQ2d 1429 (Fed. Cir. 1997).

The reference teachings anticipate the claimed invention.

14. Claims 13 and 23-24 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent Publication 2003/135888. (PTO-892, Reference A).

U.S. Patent Publication 2003/135888 teaches the polypeptide of SEQ ID NO:298, which has 47.4% similarity to instant SEQ ID NO:2, with 252 matches, 82 conservative substitutions 145 non-conservative substitutions, and 9 gaps (In particular, see attached sequence alignmen, claim 7t). The cysteine at position 50 in SEQ ID NO:2 has been changed to a glycine. Claims 13 and 23-24 read on the reference polypeptide of SEQ ID NO:298 because it is "a polypeptide comprising a mutation, elimination or addition of at least on amino acids residue in the polypeptide sequence of SEQ ID NO:2, 4 or 6" and "a polypeptide which is encoded by a polynucleotide sequence which hybridizes to the complement of the polynucleotide sequences in (c) under stringent condition and originates from DNA sequences of Poaceae species" that reads on derivates and fragments of SEQ ID NO:2.

The limitations "the polypeptide according to Claim 13 (b), wherein said mutation results in the replacement of at least one cysteine residue of a polypeptide whose sequence is set forth in SEQ ID NO: 2, SEQ ID NO: 4 or SEQ ID NO: 6 with another amino acid residue" of claim 23;

and "the polypeptide according to Claim 13 (d), which comprises replacement of at least one cysteine residue of the polypeptide which is encoded by a polynucleotide whose sequence is set forth in SEQ ID NO: 1, SEQ ID NO: 3 or SEQ ID NO: 5 with another amino acid residue" of claim 24 are inherent features of the polypeptide of reference SEQ ID NO:298.

The reference teachings anticipate the claimed invention.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

November 14, 2007

Nora M. Rooney, M.S., J.D.

Patent Examiner

Technology Center 1600

Maher M. Haddad

MAHER M. HADDAD
PRIMARY EXAMINER